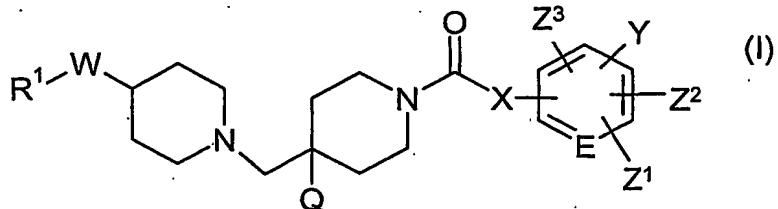


CLAIMS

1. A compound of formula (I):



5

wherein:

E is CH or N;

Q is hydrogen or hydroxy;

W is CH<sub>2</sub>, O or NR<sup>2</sup>;

X is a bond, CH<sub>2</sub> or CH<sub>2</sub>O;

10 Y is OH, CO<sub>2</sub>R<sup>3</sup>, SO<sub>3</sub>H, CH<sub>2</sub>CO<sub>2</sub>R<sup>3</sup>, CH<sub>2</sub>SO<sub>3</sub>H, OCH<sub>2</sub>CO<sub>2</sub>R<sup>3</sup> or OCH<sub>2</sub>SO<sub>3</sub>H;

Z<sup>1</sup>, Z<sup>2</sup>, Z<sup>3</sup> are, independently, hydrogen, halogen, cyano, nitro, hydroxy, NR<sup>4</sup>R<sup>5</sup>, C<sub>1-6</sub> alkyl (optionally substituted with halogen), C<sub>1-6</sub> alkoxy (optionally substituted with halogen), S(O)<sub>p</sub>(C<sub>1-6</sub> alkyl), S(O)<sub>q</sub>CF<sub>3</sub> or S(O)<sub>2</sub>NR<sup>6</sup>R<sup>7</sup>;

15 R<sup>1</sup> is phenyl optionally substituted by halogen, cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>1-4</sub> alkoxy or C<sub>1-4</sub> haloalkoxy;

R<sup>2</sup> is hydrogen or C<sub>1-4</sub> alkyl;

R<sup>3</sup> is hydrogen, C<sub>1-6</sub> alkyl or benzyl;

p and q are, independently, 0, 1 or 2;

20 R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are, independently, hydrogen, C<sub>1-6</sub> alkyl (optionally substituted by halogen, hydroxy or C<sub>3-10</sub> cycloalkyl), CH<sub>2</sub>(C<sub>2-5</sub> alkenyl), phenyl (itself optionally substituted by halogen, hydroxy, nitro, NH<sub>2</sub>, NH(C<sub>1-4</sub> alkyl), N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring as described for R<sup>4</sup> and R<sup>5</sup> below),

S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>NH<sub>2</sub>, S(O)<sub>2</sub>NH(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring as described for R<sup>4</sup> and R<sup>5</sup> below), cyano, C<sub>1-4</sub>

25 alkyl, C<sub>1-4</sub> alkoxy, C(O)NH<sub>2</sub>, C(O)NH(C<sub>1-4</sub> alkyl), C(O)N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring as described for R<sup>4</sup> and R<sup>5</sup> below), CO<sub>2</sub>H,

CO<sub>2</sub>(C<sub>1-4</sub> alkyl), NHC(O)(C<sub>1-4</sub> alkyl), NHS(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), C(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub> or OCF<sub>3</sub>) or heterocyclyl (itself optionally substituted by halogen, hydroxy, nitro,

NH<sub>2</sub>, NH(C<sub>1-4</sub> alkyl), N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring

as described for R<sup>4</sup> and R<sup>5</sup> below), S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>NH<sub>2</sub>, S(O)<sub>2</sub>NH(C<sub>1-4</sub> alkyl), S(O)<sub>2</sub>N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring as described for R<sup>4</sup> and R<sup>5</sup> below), cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C(O)NH<sub>2</sub>, C(O)NH(C<sub>1-4</sub> alkyl), C(O)N(C<sub>1-4</sub> alkyl)<sub>2</sub> (and these alkyl groups may join to form a ring as described for R<sup>4</sup> and R<sup>5</sup> below), CO<sub>2</sub>H, CO<sub>2</sub>(C<sub>1-4</sub> alkyl), NHC(O)(C<sub>1-4</sub> alkyl), NHS(O)<sub>2</sub>(C<sub>1-4</sub> alkyl), C(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub> or OCF<sub>3</sub>);  
5 alternatively NR<sup>4</sup>R<sup>5</sup> or NR<sup>6</sup>R<sup>7</sup> may, independently, form a 4-7 membered heterocyclic ring, azetidine, pyrrolidine, piperidine, azepine, morpholine or piperazine, the latter optionally substituted by C<sub>1-4</sub> alkyl on the distal nitrogen;  
10 or an N-oxide thereof; or a pharmaceutically acceptable salt thereof; or a solvate thereof.

2. A compound of formula (I) as claimed in claim 1 wherein W is O.

15 3. A compound of formula (I) as claimed in claim 1 or 2 wherein E is CH.

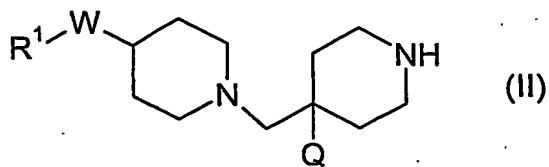
4. A compound of formula (I) as claimed in claim 1, 2 or 3 wherein R<sup>1</sup> is phenyl optionally substituted with halogen, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> alkoxy.

20 5. A compound of formula (I) as claimed in claim 1, 2, 3 or 4 wherein Y is CO<sub>2</sub>H, CO<sub>2</sub>(C<sub>1-4</sub> alkyl), CH<sub>2</sub>CO<sub>2</sub>H or OH.

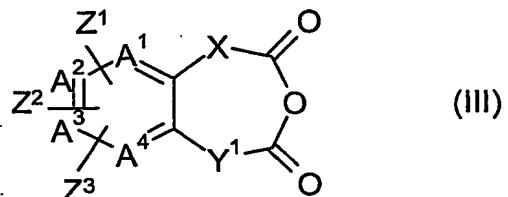
25 6. A compound of formula (I) as claimed in claim 1, 2, 3, 4 or 5 wherein Z<sup>1</sup>, Z<sup>2</sup> and Z<sup>3</sup> are, independently, hydrogen, halogen, cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, CF<sub>3</sub>, OCF<sub>3</sub>, S(O)<sub>2</sub>(C<sub>1-4</sub> alkyl) or S(O)<sub>2</sub>NH<sub>2</sub>.

7. A process for preparing a compound of formula (I) as claimed in claim 1, the process comprising:

30 a. when Y is CO<sub>2</sub>H, CH<sub>2</sub>CO<sub>2</sub>H or OCH<sub>2</sub>CO<sub>2</sub>H, said Y group being ortho to the group X, acylating a compound of formula (II):

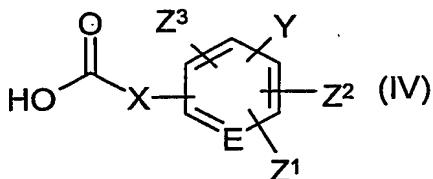


via the ring opening of an anhydride of formula (III):



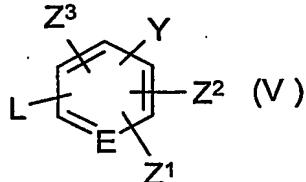
wherein one of A¹, A², A³ and A⁴ is CH or N; the other three of A¹, A², A³ and A⁴ are carbon and each of the three carries Z¹, Z² or Z³, there being only one of each of Z¹, Z² and Z³; X is as defined in claim 1; and Y¹ is a bond, CH₂ or OCH₂; in the presence of a suitable tertiary amine, in a suitable solvent at an elevated temperature;

5 b. when Y is CO₂R³, CH₂CO₂R³ or OCH₂CO₂R³ and R³ is not hydrogen, coupling a compound of formula (II) with a compound of formula (IV):



either going via the acid chloride of the compound of formula (IV) or by using a coupling reagent;

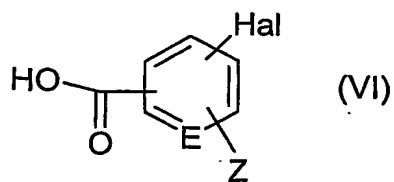
10 c. when X is a bond and Y is CO₂R³, carbonylating a compound of formula (V):



15 wherein L is chloro, bromo, iodo or O-triflate, and then quenching the product so formed with a compound of formula (II);

d. when X is a bond, Y is CO₂R³, R³ is not hydrogen, and R¹ does not have a chloro, bromo or iodo substituent,

20 i. coupling a compound of formula (II) with an acid of formula (VI):



wherein Hal is chloro, bromo or iodo;

- 5           ii. carbonylating the compound so formed; and then,
- iii. quenching the product so formed with a C<sub>1-6</sub> aliphatic alcohol or benzylalcohol;

OR

- 10           e. when Y is or includes a CO<sub>2</sub>R<sup>3</sup> group:
  - i. when R<sup>3</sup> is hydrogen said compound can be converted to a compound of the invention where R<sup>3</sup> is not hydrogen by a standard esterification method; or
  - ii. when R<sup>3</sup> is not hydrogen said compound can be converted to a compound of the invention where R<sup>3</sup> is hydrogen by a standard ester hydrolysis method.

15       8. A pharmaceutical composition which comprises a compound of the formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, and a pharmaceutically acceptable adjuvant, diluent or carrier.

20       9. A compound of the formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, for use in therapy.

25       10. A compound of formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1, in the manufacture of a medicament for use in therapy.

30       11. A method of treating a chemokine mediated disease state in a mammal suffering from, or at risk of, said disease, which comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof or solvate thereof as claimed in claim 1.